

REMARKS

Claims 1-7 and 16-17 are pending and under consideration.

The Examiner states that the application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825 for applications containing nucleotide and/or amino acid sequences. Specifically, the Examiner contends that the nucleic acid sequences on pp. 51-52 of the instant specification are not identified by unique sequence identifiers.

Claims 1-7 and 16-17 are rejected under the second paragraph of 35 U.S.C. § 112 as being indefinite for a variety of reasons, including lack of proper antecedent basis and a lack of clarity of certain terms contained within these claims.

Claims 1-2, 6-7 and 16 are rejected under 35 U.S.C. § 102(b) as being anticipated by Caetano-Anolles *et al.* (WO95/33853).

For reasons set forth below, Applicants respectfully request that the rejections be removed and the claims be allowed to issue.

I. The Application Complies with the Requirements of 37 C.F.R. §§ 1.821-1.825

The Examiner states that the application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825 for applications containing nucleotide and/or amino acid sequences. Specifically, the Examiner contends that the nucleic acid sequences on pp. 51-52 of the instant specification are not identified by unique sequence identifiers.

With regard to compliance with the requirements for applications containing nucleotide and/or amino acid sequences, Applicants respectfully note that, in a response received by the United States Patent and Trademark Office on July 9, 2002, Applicants provided unique sequence identifiers for each of the sequences contained in Tables 1 and 2 located on pp. 51 and 52, respectively, of the

instant specification. Thus, Applicants maintain that, following the amendments made to the pending claims on February 26, 2003 in response to Examiner Tung's telephone call, the instant application is in fact in full compliance with the requirements of 37 C.F.R. §§ 1.821-1.825.

However, in the interest of facilitating the most rapid prosecution possible of the instant application, Applicants herein amend Tables 1 and 2 of the instant specification to place the sequence identifiers in a more prominent location. In light of these arguments and amendments, Applicants respectfully request that the Examiner find the specification in compliance with 37 C.F.R. § 1.821-1.825.

II. The Claims Are Definite

Claims 1-7 and 16-17 are rejected under the second paragraph of 35 U.S.C. § 112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, Claim 2 is rejected as vague and indefinite because the phrase "the single stranded DNA" is allegedly without antecedent basis. In response, Applicants have amended Claim 2 so that "DNA" has been replaced by "cDNA." Applicants maintain that the phrase "single-stranded cDNA" in Claim 2 now has clear antecedent basis in Claim 1.

Claim 7 is rejected as vague and indefinite because, according to the Examiner, the phrase "a simple stem loop structure" is allegedly unclear. Applicants respectfully disagree, because from the alternatives presented and in view of the teaching of the specification, Applicants assert that one of ordinary skill in the art would understand that a simple loop is a single hairpin-like loop, compared to a cloverleaf loop, which is a multiple loop structure. For example, hairpin (D-SLAP) and cloverleaf (D-CLAP) structures are shown in Figure 1B, where one can infer that SLAP denotes

single loop and CLAP denotes cloverleaf. See p. 36, lines 20-21 of the specification. However, in the interest of advancing the prosecution of this case, Applicants herein amend Claim 7 to recite hairpin or clover-leaf structures. Support for this amendment may be found, *inter alia*, on p. 36, lines 20-25 of the instant specification.

Claims 16-17 are rejected as vague and indefinite because the phrase "the mRNA poly-A sequence" is allegedly without antecedent basis. In response, Applicants respectfully note that, as stated in Section 2173.05(e) of the *Manual of Patent Examining Procedure*, a claim is not indefinite if it would be readily understood by one of skill in the art. Furthermore, inherent components of elements recited in the claims have antecedent basis in the recitation of the components themselves. Applicants maintain that one of ordinary skill in the art would readily comprehend that a method which recites a step in which a primer containing a poly-dT sequence is admixed with mRNA and reverse transcriptase under conditions sufficient for annealing the primer to the mRNA poly-A sequence means that the poly-dT sequence of the primer is annealing to the polyA tail of the mRNA. However, to bring greater clarity to the claim, Applicants have amended Claim 16 so that it now indicates that the mRNA of step (A)(i) is an mRNA comprising a polyA sequence.

The Examiner also notes that Claims 16-17 contain the phrase "one primer which has a sequence identical to at least a portion of the primer sequence of element [(ii)]," which the Examiner alleges is unclear. The Examiner asks whether the "one primer" of this phrase is the third primer of the method. The Examiner further asks which primer contains the portion which is identical to the sequence of the one primer. In response, Applicants have amended Claim 16 so that the gene-specific primer is recited as the second primer, the primer which has a sequence identical to at least a portion of the primer sequence of element (ii) is recited as the third primer, and the primer sequence of element (ii) is recited as the first primer. Applicants maintain that these amendments should render

Claims 16-17 definite.

Claims 1-7 are rejected as vague and indefinite because, according to the Examiner, the identities of the fifth and sixth sequences in the third primer were unclear. In response, Applicants have amended Claim 1 such that the fifth and sixth sequences referred to in step (C)(iii) have been identified as the first and second sequences of the third primer.

In light of the amendments made to the claims and the arguments provided herein, Applicants respectfully request that the rejections of Claims 1-7 and 16-17 under the second paragraph of 35 U.S.C. § 112 be withdrawn and the claims be allowed to issue.

III. The Claims Are Not Anticipated

The Examiner rejects Claims 1-2, 6-7 and 16 under 35 U.S.C. §102(b) as being anticipated by the PCT application of Caetano-Anolles *et al.* (WO95/33853). According to the Examiner, Caetano-Anolles *et al.* disclose a method of DNA amplification fingerprinting using at least one primer that recognizes an arbitrary region of the DNA template, wherein said primer comprises a hairpin structure at its 5' end. The Examiner further alleges that Caetano-Anolles *et al.* teach that the amplification reaction may utilize multiple primers for increased yield, and that either RNA or DNA molecules may serve as templates. When RNA is used as a template, the primer comprises a polyT sequence and reverse transcriptase is employed to generate the first DNA strand. The primers employed in the method of Caetano-Anolles *et al.* also may incorporate inosine. Based on these features, the Examiner concludes that Caetano-Anolles *et al.* anticipates Claims 1-2, 6-7 and 16 of the instant application.

In response, Applicants first note that Caetano-Anolles *et al.* teach methods for DNA fingerprinting. As stated in Caetano-Anolles *et al.*, DNA fingerprinting is the "enzymatic

amplification of *arbitrary stretches* of DNA which is directed by short oligonucleotide primers of *arbitrary sequence* to generate complex but characteristic DNA fingerprints." Caetano-Anolles *et al.*, p. 2 (emphasis added). The goal of DNA fingerprinting is the maximization of the polymorphic informational content ("PIC") of the sample through the amplification of as many DNA fragments as possible in a single reaction. In contrast, the instant application teaches methods for isolating full-length cDNA clones from partial cDNA fragments of known sequence. The desired goal is the amplification of a single DNA fragment that is specific for the gene of interest.

Because these two inventions have different goals, it is not surprising that they use different methodologies in achieving these goals. For example, as noted by Caetano-Anolles *et al.* on pp. 14-15 of their application, DNA amplification fingerprinting using *arbitrary* mini-hairpin oligonucleotides is carried out by using one or more of the *arbitrary* mini-hairpin oligonucleotides to randomly amplify a DNA template. No primers with target gene-specific sequences are used; nor would one of ordinary skill in the art want to modify the teachings of Caetano-Anolles *et al.* to incorporate a gene specific primer, because such a modification would be counterproductive to the goal of this method, which is to maximize the informational content of the fingerprint through the amplification of as large a number of bands as possible.

In contrast, the instant application teaches the specific amplification of a desired complete open reading frame using one arbitrary primer and one gene-specific primer in a first round of amplification (first and second primers of Claim 1) followed by a second round of amplification using one gene-specific primer and a primer specific for sequence contained in the hairpin region of the first primer (second and third primers of Claim 1). While the arbitrary primer, in certain embodiments, does contain a hairpin element, this is the only similarity with the teachings of Caetano-Anolles *et al.* The use of additional gene- and primer-specific primers to specifically

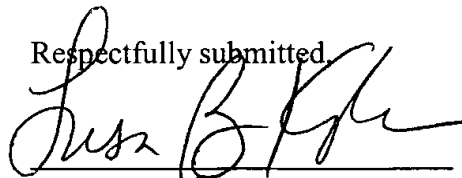
amplify a desired DNA sequence containing an open reading frame is not disclosed, either expressly nor inherently, in the teachings of Caetano-Anolles *et al.* Thus, Applicants maintain that Caetano-Anolles *et al.* do not anticipate Claim 1 or the claims dependent therefrom (Claims 2, 6-7 and 16), and respectfully request that the Examiner withdraw the rejection of these claims under 35 U.S.C. § 102(b).

CONCLUSION

Based on the foregoing remarks and in light of the amendments, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is therefore respectfully requested.

Applicants believe a fee of \$205.00 is due with this response for a two-month extension of time as required under 37 C.F.R. §1.17(a)(2) and, accordingly, Applicants enclose a check in the amount of \$205.00. Should any additional fees be required in association with this communication or should any overpayment be made, the Commissioner is hereby authorized to charge an additional fees or credit any overpayments to Deposit Account Number 02-4377. A duplicate copy of this communication is enclosed.

Respectfully submitted,



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Enclosure